

## REMARKS

Claims 1-44 are in this application. Claims 36-44 have been added. Claims 36-44 define a method of treating a subject with a bacterial infection. Support for these claims is found in original claims 24-32 which have now been amended to define a method for prophylactic treatment.

According to the Official Action, claims 1-10, 12, 14, 15, 22, 24, 26, 27 and 30-34 are rejected under 35 USC 102 (e) over Souza et al (US patent) 6,514,986. This is respectfully traversed.

The '986 patent discloses a substantially crystalline form and amorphous forms of the arginine salt of S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j] quinolizine-2-carboxylic acid (column 2, lines 29-34; column 8, lines 23, 47 and also column 6, lines 44-50; column 4, lines 39-40). However it does not disclose the pharmaceutical formulation of claims 1-10, 12, 14, 15, 22, 24, 26, 27 and 30-34 of this application.

Examples 1 and 2 of the '986 patent teach the art of making the salts viz. substantially crystalline form of the S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt.

The '986 patent describes the use of acids, bases, and organic basic salts to make the salts of S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid. This is different from the invention claimed in this application. In the present application the pharmaceutically compositions comprise (a) a benzoquinolizine-2-carboxylic acid antimicrobial drug or salt, polymorphic form, enantiomeric form, other isomeric or racemic form thereof in a **therapeutically or prophylactically effective drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH, and (b) a pharmaceutically acceptable solubilizing agent selected from a basic amino-acid, a cyclodextrin, a cyclodextrin polymer or derivative thereof or a mixture thereof in a concentration sufficient to maintain the drug in solution at a drug concentration that is above the practical limit of**

**solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH. (emphasis added).**

This composition is not anticipated by the '986 patent because the '986 patent does not disclose a therapeutically or prophylactically effective drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH and use of a ) a pharmaceutically acceptable solubilizing agent selected from a basic amino-acid, a cyclodextrin, a cyclodextrin polymer or derivative thereof or a mixture thereof in a concentration sufficient to maintain the drug in solution at a drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH.

In the claimed invention, a solubilizing agent selected from a basic amino acid, a cyclodextrin, a cyclodextrin polymer or derivative thereof is used to maintain the drug in solution at a drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH. The use of solubilizing agent is clearly different from what is described in the '986 patent where Souza et al. teach a method for preparing a salt, i.e. S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid arginine salt, and not an aqueous pharmaceutical composition that is suitable for different uses such as for parenteral administration.

Anticipation requires that each and every element of the claimed invention be disclosed in a single prior art reference. *In re Paulsen*, 30 F.3d 1475, 31 USPQ 1671 (Fed. Cir. 1994) and that there must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Res. Found. v. Genentech, Inc.*, 927 F.2d 1565, 18 USPQ2d 1001 (Fed. Cir. 1991). Since every element of the claimed invention is not found in the '968 patent, it is respectfully requested that this rejection be withdrawn.

According to the Official Action claims 11 and 12 are rejected under 35 USC 102 (e) over Souza et al (US patent application publication 2002/0177559). This is respectfully traversed.

Claims 11 and 12 depend indirectly from claim 1 therefore, all of the limitations of claim 1 are considered to be incorporated into claims 11 and 12.

While example 21 on page 28 of the Souza et al (US patent application publication 2002/0177559) describes preparation of a hydrate i.e. S-(-)-9-fluoro-6,7-dihydro-8-(4-hydroxypiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid 0.2 hydrate as stated above claim 11 defines a pharmaceutical composition having the features of claim 1. These features are not disclosed in the cited published application.

The compound disclosed in paragraph 168, page 9 of US patent application publication 2002/0177559 is S-(-)-9-fluoro-6,7-dihydro-8-(4'-hydroxy-3',3'-dimethylpiperidin-1-yl)-5-methyl-1-oxo-1H,5H-benzo[i,j]quinolizine-2-carboxylic acid which is not the same as the compound included in claim 12. The compound of claim 12 is not disclosed in the cited US patent application publication. Furthermore, as stated above claim 12 defines a composition which has the features of claim 1.

Therefore, since US patent application publication 2002/0177559 does not disclose all of the elements of claims 11 and 12, this publication cannot and does not anticipate claims 11 and 12.

It is respectfully requested that the rejection be withdrawn.

According to the Official Action, claims 1, 4, 5, 7, 8, 9, 23, 24, 26, 27 and 30 have been rejected under 35 USC 103 (a) over Schulz et al (US patent application publication 2003/0045544). This is respectfully traversed.

Schulz et al. teach topical and / or local treatment of compounds represented by the genus compounds.

As discussed above, claim 1 of the subject application defines a pharmaceutical composition that comprises (a) a benzoquinolizine-2-carboxylic acid antimicrobial drug salt, polymorphic form, enantiomeric form, other isomeric or racemic form thereof in a therapeutically or prophylactically effective drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH, and (b) a pharmaceutically acceptable solubilizing agent selected from a basic amino-acid, a cyclodextrin, a cyclodextrin polymer or derivative thereof or a mixture thereof in a concentration sufficient to maintain the drug in solution at a drug concentration that is above the practical limit of solubility of the drug in a substantially isotonic aqueous solution at a physiologically compatible pH.

As stated above the compositions of this invention have a number of uses and one of these uses is for parenteral administration. Schulz et al. describes topical and local treatment and does not describe or suggest pharmaceutical compositions for parenteral administration.

Furthermore, as shown in examples 1 and 4 pharmaceutical compositions according to the claims have been shown by experimental data, as having advantages such as reduced vein irritation, and reduction in the incidence of phlebitis. The compositions of this invention are suitable for administration to human or veterinary patients.

Therefore, given the differences between the disclosure of Schulz et al. and the claimed invention and furthermore, given that there is no suggestion in Schulz et al. of the claimed invention, it is respectfully requested that this rejection be withdrawn.

According to the Official Action, claim 7 is rejected under 35 USC 112, first paragraph, as not being enabling for making prodrugs of the claimed compounds. This is respectfully traversed.

The prodrugs of the claimed compounds are enabled. However, to expedite prosecution, the term prodrugs has been deleted from claim 7.

All rights to file one or more divisional and/or continuation applications for this subject matter is preserved.

Therefore, it is respectfully requested that this rejection be withdrawn.

According to the Official Action, claims 7, 8, 24 and 30 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This is respectfully traversed.

The use of the term pseudopolymorph does not make the claim indefinite. However, to expedite prosecution, the term pseudopolymorph has been deleted from claim 7.

All rights to file one or more divisional and/or continuation applications for this subject matter is preserved.

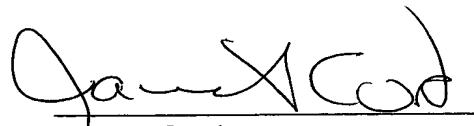
Claim 8 was amended to replace the phrase “formula (I)” with “formula (II)”. Claim 7 includes the structure of formula (II).

Claim 30 depends from claim 24 which in turn depends from claim 1. The term solubising agent is used in claim 1.

Therefore, it is respectfully requested that this rejection be withdrawn.

Accordingly, it is submitted that this application is in condition for allowance and favorable consideration is respectfully requested.

Respectfully submitted,



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